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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,400	03/30/2001	Yehuda Shoenfeld	01/21885	1174

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/806,400	SHOENFELD ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this c mmunication appears on the c ver sheet with the c rrespondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-4,8-11,14-24,26 is/are pending in the application.

4a) Of the above claim(s) 2-4,8-11,15-17 and 21-24 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 14,18-20 and 26 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The request filed on 12/17/2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No.09/806400 is acceptable and a CPA has been established. An action on the CPA follows.

2. Applicant's election of Group II in Paper No. 20 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claim 14 recites nonelected inventions (use of HSP 60/65 or B_2GP-1, see restriction requirement mailed 7/18/2001) which need to be deleted from said claim.

4. Claims 1,5-7,12,13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in Paper No. 20.

5. Claims 14,18-20,26 are under consideration. Claims 1,5-7,12,13,25 have been cancelled.

6. Regarding the IDS filed 2/27/2003, the Pech et al. reference is a French language publication which was not considered. Meir et al. was not considered because no journal of publication or citation information was supplied. The other references not considered were duplicate references.

7. The amendment filed 4/23/2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows. There is no support in the specification as originally filed for the recitation of "the composition being formulated for inducing oral tolerance" in the abstract filed with the amendment filed 4/23/2002. Regarding applicants comments about the specification, pages 15 and 16, said pages disclose a specific method for preparing oxidized LD, they do not disclose "the

composition being formulated for inducing oral tolerance". The specification and original claims disclose that the claimed invention contained oxidized LDL and a pharmaceutically acceptable carrier. The specification does not disclose that oxidized LDL requires any particular manipulation or formulation to render it tolerogenic. The limitation "the composition being formulated for inducing oral tolerance" would seem to encompass further processing of the oxidized LDL component. However, there is no disclosure in the specification as originally filed of the scope of the claimed invention which encompasses oxidized LDL being formulated for inducing oral tolerance. There is no written description of the scope of the claimed invention in the specification as originally filed (eg. the claimed invention constitutes new matter).

Applicant is required to cancel the new matter in the reply to this Office Action.

Regarding applicants comments in the amendment filed 11/29/2002, the aforementioned limitations have not been removed from the abstract.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 14,18-20,26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "wherein said administration is in a sufficient amount to induce production of TGFB, to suppress IFN-γ, and to suppress a type 1 T-cell cytokine pattern" in claim 14. Regarding applicants comments about the specification, page 3, lines 12-16, said passage refers to specific empirical observations about cytokines found in human atherosclerotic lesions in the prior art. It does not disclose the claimed method wherein said limitation defines the dosage of a tolerance inducing composition to be administered. Regarding applicants comments about the specification, page 13, lines 11-19, said passage

discloses that a possible mechanism of tolerance is stimulation and production of TGFB and the development of non-specific suppressor cells. The aforementioned is a statement of a hypothetical mechanism of action, not a dosage of a tolerance inducing composition to be administered. In addition, said passage does not disclose "suppress IFN-γ, and to suppress a type 1 T-cell cytokine pattern". There is no written description of the scope of the claimed invention in the specification as originally filed (eg. the claimed invention constitutes new matter).

10. Claims 14,18-20,26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the claimed method of preventing or treating atherosclerosis using an oral tolerance inducing dosage of modified LDL or OxLDL.
The specification does not disclose how to use the claimed method in vivo in humans to treat or prevent disease. Applicant has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the instant invention disclosed in the specification is the treatment or prevention of disease in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence as to how the instant invention could be used for preventing or treating atherosclerosis using an oral tolerance inducing dosage of modified LDL or OxLDL.
Judge Lourie stated in Enzo Biochem Inc. v. Calgene Inc. CAFC 52 USPQ2d 1129 that:

The statutory basis for the enablement requirement is found in Section 112, Para. 1, which provides in relevant part that:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. . . .
35 U.S.C. Section 112, Para. 1 (1994). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed

invention without 'undue experimentation.' " Genentech, Inc. v. Novo Nordisk, A/S , 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright , 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see Hybritech, Inc. v. Monoclonal Antibodies, Inc. , 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), which in this case is October 20, 1983 for both the '931 and '149 patents. 8

We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g., Wands , 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In In re Wands , we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See Amgen, Inc. v. Chugai Pharm. Co., Ltd. , 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the Wands factors "are illustrative, not mandatory. What is relevant depends on the facts.").

Regarding Wands factors (4) and (8), the claims encompass treatment or prevention of atherosclerosis in vivo in humans. Regarding Wands factors (5) and (7), there is a high degree of unpredictability in the art. For example, Spack teaches that attempts to treat MS via inducing oral tolerance to myelin protein have been unsuccessful (see abstract). Similarly, the art recognizes that attempts to treat rheumatoid arthritis via inducing oral tolerance to collagen have been unsuccessful (see McKown et al.). Thus, it is

recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. Regarding Wands factor (3), while the specification provides an example in a mouse model, there were copious amounts of mouse research that suggested that oral tolerance could be used to treat MS or rheumatoid arthritis, yet said diseases were not successfully treated in humans using oral tolerance. Regarding Wands factor (2), there is no disclosure in the specification as to what doses would be used to induce the functional parameters recited in the claim which are related to properties of the oral tolerance induction mechanism.
Based on the aforementioned undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification.

11. Regarding the term "modified LDL", applicant has indicated that the meaning of said term is as per used in the prior art such as US Patent 5,409,710. US Patent 5,409,710 provides a definition of said term on column 5, second paragraph.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 14,18,20 stand rejected under 35 U.S.C. 102(b) as being anticipated by Yesair et al. (US Patent 4,874,7695) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Yesair et al. teach a composition for oral administration containing LPC (see column 5, last paragraph and Examples). LPC is also a derivative of Ox LDL (see specification, page 5, first complete paragraph). LPC is a modified LDL. The pharmaceutically acceptable carrier is the other lipids contained in the composition taught by Yesair et al. (see column 5). Yesair et al. teach the in vivo administration of said composition (see Examples and column 13, last paragraph). It is an inherent property that administration of the claimed composition results in the method of claim 14, because the method taught by Yesair et al. involves administration of the same

compound (LPC) to the same population (eg. any individual, because it would be desirable to prevent atherosclerosis in any individual). Regarding the functional properties as pertaining to the dosage recited in claim 14, there is no disclosure in the specification as to a particular range or concentration of the administered agent that would result in the functional activities. Therefore it will be assumed for the purposes of prior art that the dose is not relevant or critical to said properties.

Regarding applicants comments, neither the Shen et al. nor the Maurer et al. references address the issue of oral tolerance. Regarding applicants comments about pages 15 and 16 of the specification, there is no evidence of record that the method used to prepare oxidized LDL is anything other than the art recognized method to prepare oxidized LDL. Regarding applicants comments about oral tolerance and the compound taught by Yesair et al.,
the MPEP section 716.01(c), page 700-217 (August 2001) states:

ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

There is no evidence of record that the composition taught by Yesair would not induce oral tolerance. The specification discloses that Ox LDL can be used to induce oral tolerance. It does not disclose that Ox LDL has to be administered in any particular form to induce oral tolerance.

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the

Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

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Art Unit 1644